

AMENDMENTS TO THE SPECIFICATION:

On page 1, please **delete** the paragraph entitled "Cross Reference to Related Applications" and replace it with the following paragraph.

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CROSS REFERENCE TO RELATED APPLICATIONS

A<sup>1</sup>  
This application claims priority under 35 U.S.C. § 119(e) ~~to~~ of U.S. Provisional Application No. 60/202,213 filed May 8, 2000, and under 35 U.S.C. § 120 **as a Continuation-in-Part** of U.S. ~~Appln.~~ **Application** Serial Nos. 09/654,617, filed September 5, 2000, and **as a Continuation-in-Part of Appln. No.** 09/684,016, filed October 10, 2000, the disclosures of which applications are incorporated herein by reference in their entirety.

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On page 5, lines 12-20, please **delete** the paragraph beginning "[s]imilarity analysis includes database...." and replace it with the following paragraph.

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A<sup>2</sup>  
Similarity analysis includes database search and alignment. Examples of public databases include the DNA Database of Japan (DDBJ) (~~www-ddbj.nig.ac.jp/~~) (~~www.ddbj.nig.ac.jp/~~); Genbank (**www-ncbi.nlm.nih.gov/web/Genbank/Index.html**) (~~www.ncbi.nlm.nih.gov/web/Genbank/Index.html~~); and the European Molecular Biology Laboratory Nucleic Acid Sequence Database (EMBL) (**www-ebi.ac.uk/ebi docs/embl db.html**) (~~www.ebi.ac.uk/ebi docs/embl db.html~~). A number of different search algorithms have been developed, one example of which are the suite of programs referred to as BLAST programs. There are five implementations of BLAST, three designed for nucleotide sequences queries (BLASTN, BLASTX, and TBLASTX) and two designed for protein sequence queries (BLASTP and TBLASTN) (Coulson, *Trends in Biotechnology*, 12:76-80 (1994); Birren, *et al.*, *Genome Analysis*, 1:543-559 (1997)).

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On page 7, lines 3-19, please **delete** the paragraph beginning “[h]omologues in other organisms....” and replace it with the following paragraph.

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13  
Homologues in other organisms are available that can be used for comparative sequence analysis. Multiple alignments are performed to study similarities and differences in a group of related sequences. CLUSTAL W is a multiple sequence alignment package available that performs progressive multiple sequence alignments based on the method of Feng and Doolittle, *J. Mol. Evol.* 25:351-360 (1987), the entirety of which is herein incorporated by reference. Each pair of sequences is aligned and the distance between each pair is calculated; from this distance matrix, a guide tree is calculated, and all of the sequences are progressively aligned based on this tree. A feature of the program is its sensitivity to the effect of gaps on the alignment; gap penalties are varied to encourage the insertion of gaps in probable loop regions instead of in the middle of structured regions. Users can specify gap penalties, choose between a number of scoring matrices, or supply their own scoring matrix for both the pairwise alignments and the multiple alignments. CLUSTAL W for UNIX and VMS systems is available at: **ftp-ebi.ac.uk** ~~ftp-ebi.ac.uk~~. Another program is MACAW (Schuler et al , *Proteins, Struct. Func. Genet.* 9:180-190 (1991), the entirety of which is herein incorporated by reference, for which both Macintosh and Microsoft Windows versions are available. MACAW uses a graphical interface, provides a choice of several alignment algorithms, and is available by anonymous ftp at: **ncbi.nlm.nih.gov** ~~ncbi.nlm.nih.gov~~(directory/pub/macaw).

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